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rdenison@environmentaldefense.org

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To: NCIC OPPT@EPA, ChemRTK HPV@EPA, Rtk Chem@EPA, Karen Boswell/DC/USEPA/US@EPA, parodr@basf.com, NCIC HPV@EPA
cc: lucierg@msn.com, kflorini@environmentaldefense.org, rdenison@environmentaldefense.org
Subject: Environmental Defense comments on Cyclohexane, Oxidized, Aqueous Extract (CAS# 68915-38-8)

(Submitted via Internet 6/28/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and parodr@basf.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Cyclohexane, Oxidized, Aqueous Extract (CAS# 68915-38-8).

The test plan and robust summaries for cyclohexane oxidized, aqueous extract (EP-306) were submitted by BASF Corporation. EP-306 is a mixture apparently comprised of 13 defined chemicals and several other chemicals not specifically identified in the test plan. Most of the constituents appear to be diacids, with adipic acid and 6-hydroxycaproic acid found in the highest concentrations. EP-306 also contains cyclohexanol, cyclohexanone and cyclohexyl hydroperoxide. No chemical structures are provided in the test plan and robust summaries. This is problematic because the sponsor frequently refers to data from individual constituents for the purpose of using such data to represent the entire mixture; structures need to be provided for the constituents of this mixture

EP-306, according to the test plan, is stored at the site of manufacture and 70% is used at that site in the manufacture of 1,6-hexanediol. However, 30% of EP-306 is sent to an onsite deep well facility for disposal. What is the long term fate of EP-306 in this site? Does the hexanediol product contain any residual constituents of EP-306?

The sponsor contends that existing data are adequate to meet the requirements of the HPV program for all SIDS endpoints. This contention relies heavily on the use of surrogate data for adipic acid, one of the main constituents of EP-306. In particular, the surrogate data are proposed for repeat dose, reproductive, developmental and genetic toxicity. However, the information provided in the test plan and robust summaries is inadequate to justify use of the surrogate data, so at this time we do not concur that the four endpoints listed above have acceptable data. Although we agree that EP-306 probably does not possess significant toxic properties, the following issues need to be addressed before we could concur with the sponsor's proposal:

1. The sponsor states that 6-hydroxycaproic acid is metabolized to adipic acid, so the adipic acid data are a surrogate for 6-hydoxycaproic acid. However, the test plan does not indicate if this metabolic step occurs rapidly, whether or not it is a major pathway or whether or not other metabolites are formed; nor are metabolic or kinetic data that would support this contention provided. In addition, the developmental and genetic toxicity data for adipic acid, referred to in the test plan, are not contained in the robust summaries, so we have no way of evaluating their adequacy.

2. The sponsor does not provide any justification for concluding that the adipic acid data are relevant for all constituents of EP-306. Of particular concern are cyclohexanol, cyclohexanone and cyclohexyl hydroperoxide. Is the contending that the mode of action for adipic acid is the same for these substances? What evidence is there to support this contention?

Existing data for the ecological toxicity endpoints appear to be adequate, as data are provided for EP-306, adipic acid and a mixture of diacids. Existing data provide evidence suggesting that the mechanism of aquatic toxicity is, in large part, related to the acidic properties of EP-306. In regard to the biodegradation studies, we note that the test plan states that the test substance was EP-306, but the robust summaries indicate that it was a dicarboxylic acid solution. The revised test plan needs to clarify this point, and the identity of the test substances need to be checked and clearly presented for all studies presented in the robust summaries.

Thank you for this opportunity to comment.

George Lucier, Ph.D.
Consulting Toxicologist, Environmental Defense

Richard Denison, Ph.D.
Senior Scientist, Environmental Defense